

ORIGINAL RESEARCH ARTICLE

The effects of preoperative milk drinking on gallbladder perforation during laparoscopic cholecystectomy

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Abstract: One of the complications of laparoscopic cholecystectomy (LC) is gallbladder perforation during surgery. Fasting before surgery causes gallbladder distention, which may increase the chance of iatrogenic gallbladder perforation during LC. A fatty meal stimulates endogenous cholecystokinin release and, consequently, the gallbladder contraction. This study evaluates the effects of preoperative milk drinking on gallbladder distention and iatrogenic gallbladder perforation during LC. This study was performed on patients who were candidates for elective LC in a university hospital from March 2011 to March 2012. Patients were randomly divided into two equal groups. The case group drank 300 mL of cold full-fat pasteurized cow's milk, while the control group drank 300 mL of cold water as the placebo, six hours before LC surgery. Data were collected in a questionnaire and analyzed using descriptive statistical tests, t-test, and ANOVA analysis. In the 260 patients, despite a lack of significant differences in demographic and risk factors for gallbladder perforation between the two groups, both distention and gallbladder perforation rates were significantly lower in the case group than in the control group ($P = 0.001$ and $P = 0.032$, respectively). Thus, drinking cold full-fat pasteurized cow's milk before LC surgery can reduce gallbladder distention and, consequently, the risk of gallbladder perforation during LC.

Keywords: Cholecystectomy; laparoscopic; gallbladder diseases; iatrogenic gallbladder perforation; gallbladder distention

Introduction

Since laparoscopic techniques have been used for general surgical procedures, many reports describing a vast array of complications have been published. Although the most common complication reported with laparoscopic cholecystectomy (LC) is wound infection, the most common technical complication is the perforation of gallbladder and the spread of bile juice and gall stones into the peritoneal cavity. Gallbladder perforation during surgery has several causes; traction and repetitive grasping may tear the wall of the gallbladder, and it may also be inadvertently penetrated during dissection from the hepatic fossa with a cautery.

When fatty foods enter the stomach and intestines, the foods stimulate the release of endogenous cholecystokinin, which causes gallbladder contraction and bile excretion. A patient scheduled for surgery must fast for

six hours prior to the operation. The lack of food passage through the gut lumen reduces the release of cholecystokinin and other gut peptides. This results in gallbladder hypomotility which promotes cholestasis, inefficient gallbladder emptying, and the resulting gallbladder distention. In this case, grasping, maneuvering, or separating the gallbladder from the liver increases the probability of perforation during the surgical procedure. Pain from both wounds and intra-abdominal infections^[1] increase time of surgery and patient's hospital stay^[2], while nausea and vomiting are probable consequences of this complication. Surgeons should make every effort to prevent gallbladder perforation by performing meticulous dissection during the procedure.

Since there are few studies describing the prevention of the above-described complication, a preventive strategy based on the principle of prevention prior to treatment is needed. While aspiration of a full gallbladder before dissection reduces tension on the gallbladder wall and would make dissection easier, it may cause bile spillage and is not always possible.

Exogenous cholecystokinin hormone can be used to reduce gallbladder distention. This hormone contracts the gallbladder and lowers the sphincter of Oddi tone. In several studies, the effect of exogenous cholecystokinin on gallbladder contraction

was investigated^[3-6]. However, this hormone is non-physiologic and it is not available anywhere. Maki *et al.*^[7] surveyed the effect of drinking 300 mL of milk upon emptying of the gallbladder. According to the study, the gallbladder was emptied and its volume reduced after about 10 minutes. Therefore, in our study, we decided to test the effects of preoperative drinking of 300 mL of cold full-fat pasteurized cow's milk on gallbladder distention and iatrogenic gallbladder perforation during LC.

Material and methods

This was a randomized, single-blind clinical trial approved by the Ethics Committee for Research and Technology of the university with grant number 1210. This study was performed on patients admitted to a university hospital for elective LCs from March 2011 to March 2012. Patients with acute cholecystitis were excluded from this study. Patients were randomly divided into two groups, each with 130 patients. First, we interviewed them preoperatively using a questionnaire with information on demographic characteristics, symptoms, clinical, and para-clinical signs.

The case group drank 300 mL of cold full-fat pasteurized cow's milk (3.3%), and the control group drank 300 mL of cold water as placebo, six hours before surgery. The surgeon and surgical equipment were the same in all of the operations. The procedure was performed by an experienced surgeon. The surgeon used the North American approach, including four ports and dissection with a cautery hook. All patients received prophylactic third generation cephalosporins (ceftriaxone). Postoperatively, intravenous antibiotics were administered for 24 hours to patients with perforated gallbladders. The surgeon had no information about which group each patient was in. During surgery, the status of the gallbladder with respect to being distended (more than 4 cm in the greatest transverse diameter^[8]) and/or rupture was recorded. To measure the degree of gallbladder distention, we used a suction tip scored at 4 cm as a measuring point. In cases of perforation and leakage of bile and/or dropped stones, we performed irrigation and aspiration; all efforts were made to retrieve the stones lost during LC, and patients were closely followed for 30 days. Data analysis was performed using SPSS 16 Software for descriptive statistics (*t*-test). A *P* value of < 0.05 was considered significant.

Results

In total, 260 patients were divided into two groups, each with 130 patients. Thirty patients were male and the remainder were female. The mean age was 49.42 ± 14.44 years (20–81 years old) for the case group and 49.08 ± 16.99 years (18–85 years old) for the control group. The mean body weight for the case groups was 72.49 ± 12.30 kg (37–100 kg) and 70.62 ± 16.48 kg (45–150 kg) for the control group. There were 122 (93.8%) patients with biliary colic due to stones. 6 (2.3%) had a history of pancreatitis. 76 (29.2%) of them had history of surgery.

The distribution frequency of the risk factors for gallbladder perforation in the two groups is shown in **Table 1**. The mean frequency of gallbladder distention in the case group was significantly lower than in the control group (*P* = 0.001), but the mean frequencies of the other risk factors were not significantly different.

Table 1. Distribution frequency of gallbladder perforation risk factors in the two groups

Risk factors of gallbladder perforation		Case group	Control group	<i>P</i> value
Gender	Female	120	110	0.079
	Male	10	20	
Gallbladder wall thickness(>3 mm)		22	34	0.096
Adhesion		40	44	0.691
Intraoperative bleeding		5	12	0.130
Intrahepatic gallbladder		14	20	0.358
Difficult hilar dissection		28	22	0.420
Gallbladder distention		23	48	0.001

There were 12 (9.23%) gallbladder perforations in the case group and 25 (19.23%) in the control group. Therefore, the mean occurrence of gallbladder perforation in the case group was significantly lower than in the control group (*P* = 0.032).

Perforations occurred in the following frequencies: the fundus was perforated in 12 cases, the body in 15 cases, and the

neck in 9 cases; there were multiple perforations in 1 case. No significant difference was observed between the two groups with respect to the location of the perforation ($P = 0.072$). In terms of gallbladder perforation time during surgery, 4 cases occurred while grasping, 19 cases during dissection, 9 cases during retraction, and 5 cases during retrieval. No significant difference was observed between the two groups according to the time of gallbladder perforation ($P = 0.120$).

Discussion

In this study, there were 12 (9.23%) gallbladder perforation observed in the case group and 25 (19.23%) in the control group patients. Therefore, the average number of gallbladders perforated was 14.23%. The perforation of gallbladder and the spread of bile juice and gallstones into the peritoneal cavity during LC are common, with an incidence of 13%–40%^[9].

To reduce the risk of gallbladder perforation, some technical considerations and new methods for gallbladder dissection from the liver bed were investigated.

Improvements in instrumentations including a better video system, as well as efficient cautery probe insulation, atraumatic graspers, and well-designed specimen bags were made to prevent this complication.

Often, grasping a distended gallbladder during LC is a problem. Although many surgeons have proposed technical considerations and methods for dissection to deal with this issue, there is a lack of information on how to manage this problem in published works. Based on our study, gallbladder distention increases the risk of gallbladder perforation during LC.

Zubair *et al.*^[10] showed that distension of the gallbladder increases the risk of gallbladder perforation during LC. In healthy volunteers, it has been shown that fatty meals affect the process of gallbladder emptying and refilling^[11]. Both cholecystokinin infusion and milk (fatty meal) ingestion have been used to induce gallbladder contraction in cholecystodynamic studies. Fatty meal stimulation to study gallbladder motor function has some advantages over cholecystokinin infusion. Ingesting a test meal more closely simulates normal physiological changes that accompany food ingestion. The test meal induces the release of not only endogenous cholecystokinin, but also other gastrointestinal hormones such as gastrin^[12], that affect gallbladder contraction and emptying. In addition, the fatty meal causes endogenous cholecystokinin release for a longer time.

Our results showed that preoperative drinking of 300 mL of full-fat pasteurized cow's milk can reduce the chance of gallbladder distension and perforation during LC through a mechanism of gallbladder contraction when compared to the control group ($P < 0.05$). In a study by Calik *et al.*^[1] on 200 patients, they concluded that aspiration of the gallbladder during LC could reduce the chance of gallbladder perforation. This technique may increase the duration of the operation and the risk of bile leakage. Caliskan *et al.*^[13] evaluated the effect of a solution (a combination of adrenaline, lidocaine, and normal saline) by injecting it into the gallbladder bed during LC. However, they observed no improvement in the incidence of gallbladder perforation, bleeding, or postoperative pain.

To stimulate gallbladder contraction in our study, patients were instructed to drink 300 mL of cold full-fat pasteurized milk (3.3%) six hours before surgery. Six hours of *nil per os* (NPO) after drinking the milk are required to keep the patients' NPO status for anesthesia administration purposes and to allow complete evacuation of the stomach to prevent aspiration^[14].

In a study by Mackie *et al.*^[7], the effect of milk stimulation on gallbladder motor function was evaluated. They showed that gallbladder emptying occurred 10 minutes after milk was consumed, but the gallbladder began refilling again about an hour later. It was not noted at what time the gallbladder distended again. In another study by Bobba *et al.*^[15], the effect of a high fat diet on gallbladder emptying was investigated and it was revealed that these diets can cause faster gallbladder emptying. However they, too, did not note the duration of gallbladder emptying.

The serum cholecystokinin increases and peaks after 20–30 minutes and remains elevated until the fatty meal has passed through the upper small bowel and there is no longer a stimulus for secretion. Due to its rapid metabolism (2.5 minutes serum half-life), cholecystokinin rapidly returns to baseline^[16]. The impact of a fatty meal on gallbladder refilling was also reported in a previous study that showed obvious gallbladder refilling after 60 minutes^[17].

In our study, six hours after drinking milk, 107 (82.30%) patients did not exhibit gallbladder distention. Although various factors that increase periods of gallbladder motility were not yet investigated, the significant gallbladder contraction in our

study could be attributed to the following:

- A) Digestion of cow's milk takes more time than human milk and it cannot be digested in about 10% of adults^[18].
- B) Passage of cold milk from the stomach takes about three and half hours. Hot milk will often be digested better than cold milk^[18].
- C) When milk is pasteurized, all of its valuable enzymes are destroyed contributing to the incomplete digestion of cow's milk by the human digestive system.
- D) Milk is a liquid food, but when it reaches the stomach, it is converted into finely divided solid material. Casein is curdled and precipitated in flocculent particles by rennin which is then coagulated by gastric acids. Digestion of large curdles is more difficult. Cow's milk curdles have larger particles than human milk and is therefore more difficult to digest.

It seems that incomplete digestion of cold full-fat pasteurized cow's milk and the long time required for it to pass through the human digestive system is responsible for triggering endogenous cholecystokinin releases and, consequently, the gallbladder contraction prior to surgery.

In our study, damage to the gallbladder occurred in the gallbladder body and during dissection. Additionally, there was no significant difference between the two groups. Nevertheless, a study by Aytaç *et al.*^[19] showed that most gallbladder injuries occurred during grasping and retracting of the gallbladder. In another study by Zubair *et al.*^[10], most gallbladder injuries occur during grasping and retracting of the gallbladder after diathermy in the fundus of the gallbladder.

Comparing these studies with ours, it seems that gallbladder distention is an important cause of increasing the chance of gallbladder rupture during LC. However, this rupture can happen at any time and location.

Conclusions

The use of cold full-fat pasteurized cow's milk before LC surgery can reduce distention and, consequently, the chance of gallbladder perforation during LC.

Conflict of interest

The author declares no potential conflict of interest with respect to the research, authorship, and/or publication of this article.

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References

1. Calik A, Topaloglu S, Topcu S, Turkyilmaz S, Kucuktulu U, *et al.* Routine intraoperative aspiration of gallbladder during laparoscopic cholecystectomy. *Surg Endosc* 2007; 21(9): 1578–1581. doi: 10.1007/s00464-006-9159-7.
2. Hui TT, Giurgiu DI, Margulies DR, Takagi S, Iida A, *et al.* Iatrogenic gallbladder perforation during laparoscopic cholecystectomy: Etiology and sequelae. *Am Surg* 1999; 65(10): 944–948.
3. Krishnamurthy GT, Bobba VR, Kingston E. Radionuclide ejection fraction: A technique for quantitative analysis of motor function of the human gallbladder. *Gastroenterology* 1981; 80(3): 482–490.
4. Nora PF, Davis RP, Fernandez MJ. Chronic acalculous gallbladder disease: A clinical enigma. *World J Surg* 1984; 8(1): 106–112. doi: 10.1007/BF01658378.
5. Pomeranz IS, Shaffer EA. Abnormal gallbladder emptying in a subgroup of patients with gallstones. *Gastroenterology* 1985; 88(3): 787–791.
6. Krishnamurthy GT, Bobba VR, McConnell D, Turner F, Mesgarzadeh M, *et al.* Quantitative biliary dynamics: Introduction of a new noninvasive scintigraphic technique. *J Nucl Med* 1983; 24(3): 217–223.
7. Mackie CR, Baxter JN, Grime JS, Hulks G, Cuschieri A. Gall bladder emptying in normal subjects—A data base for clinical cholescintigraphy. *Gut* 1987; 28(2): 137–141. doi: 10.1136/gut.28.2.137.

8. Bricault I. Infections of the right hypochondrium. *Diagn Interv Imaging* 2012; 93(6): 453–465. doi: 10.1016/j.diii.2012.04.005.
9. Zulfikaroglu B, Ozalp N, Mahir Ozmen M, Koc M. What happens to the lost gallstone during laparoscopic cholecystectomy? *Surg Endosc* 2003; 17(1): 158.
10. Zubair M, Habib L, Mirza MR, Channa MA, Yousuf M. Iatrogenic gall bladder perforations in laparoscopic cholecystectomy: An audit of 200 cases. *Mymensingh Med J* 2010; 19(3): 422–426.
11. Pallotta N. Ultrasonography in the assessment of gallbladder motor activity. *Dig Liver Dis* 2003; 35(Suppl 3): S67–S69. doi: 10.1016/S1590-8658(03)00098-7.
12. Krishnamurthy GT, Bobba VR, Kingston E. Optimization of octapeptide of cholecystokinin (OP-CCK) dose for gallbladder emptying. In: Raynaud C (editor). *Proceeding of the 3rd World Congress of Nuclear Medicine and Biology*. Paris: Pergamon Press; 1982. p. 2244–2247.
13. Caliskan K, Nursal TZ, Yildirim S, Moray G, Torer N, *et al*. Hydrodissection with adrenaline-lidocaine-saline solution in laparoscopic cholecystectomy. *Langenbecks Arch Surg* 2006; 391(4): 359–363. doi: 10.1007/s00423-006-0049-1.
14. American Society of Anesthesiologists Committee on Standards and Practice Parameters. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: Application to healthy patients undergoing elective procedures: A report by the American Society of Anesthesiologist Task Force on Preoperative Fasting. *Anesthesiology* 1999; 90(3): 896–905.
15. Bobba VR, Krishnamurthy GT, Kingston E, Turner FE, Brown PH, *et al*. Gallbladder dynamics induced by a fatty meal in normal subjects and patients with gallstones: Concise communication. *J Nucl Med* 1984; 25(1): 21–24.
16. Thompson JC, Fender HR, Ramus NI, Villar HV, Rayford PL. Cholecystokinin metabolism in man and dogs. *Ann Surg* 1975; 182(4): 496–504. doi: 10.1097/0000658-197510000-00015.
17. Jonderko K, Nowak A, Kasicka-Jonderko A, Błaszczyńska M. Effect of cigarette smoking on gallbladder emptying and filling in man. *Am J Gastroenterol* 1994; 89(1): 67–71.
18. Davis NS. Milk and milk products. Part 3. Milk digestion. 2nd ed. In: *Food in health and disease* [Internet]. Philadelphia, USA: P. Blakiston's Son & Co.; 1912 [cited 2016 Jun 14]. Available from: <http://chestofbooks.com/health/nutrition/Disease-Food/Milk-And-Milk-Products-Part-3-Milk-Digestion.html>
19. Aytaç B, Çakar S. The outcome of gallbladder perforation during laparoscopic cholecystectomy. *Acta Chir Belg* 2003; 103(4): 388–391. doi: 10.1080/00015458.2003.11679449.